REMARKS

Status of the claims

Claims 11-21 and 26 are pending in the present application. Claims 1-10 and 22-25 have been cancelled. Claims 12 and 21 are amended herein. New claim 26 has been added, which incorporates the subject matter deleted from claim 12.

Rejections under 35 U.S.C.§112, 2nd paragraph

Claims 11 and 21 have been rejected under 35 U.S.C.§112, 2nd paragraph as being indefinite. More specifically, claim 11 has been rejected for recitation of a narrow range, which falls within a recited broad range of the same claim. Claim 11 has been amended to delete the overlapping narrow range and the deleted subject matter has been added new claim 26. Withdrawal of the rejection has been respectfully requested.

Claim 21 has been rejected as being unclear in meaning of the term "% by weight", with the assertion that the term is relative. Claim 21 has been amended to clarify that the "% by weight" is relative to the total weight. As such, withdrawal of the rejection is respectfully requested.

Rejections under 35 U.S.C.§103

Claims 11-21 have been rejected under 35 U.S.C.§103 as being obvious over Van Hees et al. (2002) combined with Van Hees (1999) and Junco. Van Hees (2002) is asserted to teach the preparation of complexes of piroxicam and ß-cyclodextin using super-critical CO_2($SCCO_2$), along with the inclusion of an active substance with poor aqueous solubility and a host molecule in a dense pressurized fluid. The process of Van Hees (2002) is asserted to use a method as disclosed in Van Hees (1999).

Van Hees (2002) is asserted to differ from the instant invention by failing to teach the inclusion of one or more diffusion agents as recited in the claims. Van Hees (2002) is also noted as failing to disclose the step of recovering the active substance/host molecule complex formed prior to mixing with the agent for interaction with the complex and the subsequent recovery of the thus formed soluble inclusion compound.

Junco is asserted to teach the complexation of a pharmaceutically active substance with ß-cyclodextrin using super-critical CO_2. Junco is further asserted to teach the use of co-solvents with the super-critical fluid to effect the solvent power.

The Examiner asserts that it would have been obvious to include the co-solvents of Junco with the processes of Van Hees (2002)/(1999). The Examiner further asserts that the steps of recovering the active substance/host molecule complex prior to adding the agent for interaction with the complex and subsequently recovering the soluble inclusion compound is merely an obvious selection of order of steps. Finally, the Examiner notes that the Van Hees (2002) discloses that supercritical ammonia (as used in the comparative examples of the specification) is extremely corrosive for a reactor, thus the improved yield demonstrated in the specification examples is not unexpected. Applicants traverse this rejection and withdrawal thereof is respectfully requested.

The instant invention, as encompassed by claim 11, is directed to

> 11. A process for the preparation of a soluble inclusion compound comprising one or more active substances included in one or more host molecules, the active substance or substances not being very soluble in an aqueous medium, wherein it comprises the following successive stages:
> a. bringing one or more active substances into contact with one or more host molecules,
> b. carrying out a stage of molecular diffusion by bringing a dense pressurized fluid into contact, in static mode, with the mixture obtained in stage (a) in the presence of one or more diffusion agents,
> c. recovering the active substance/host molecule molecular complex thus formed,
> d. carrying out a stage which consists in adding to and mixing with the active substance/host molecule molecular complex an agent for interaction with the complex,
> e. recovering the soluble inclusion compound thus formed.

Thus, the present invention effectively requires two steps, with the addition of the agent of interaction being carried out after the formation of the complex. Contrary to the assertion of the Examiner, the instant invention differs from the prior art not merely in an "order of the steps". The instant invention has an additional step, i.e. is a two-step process, whereas the prior art only uses a single step process. Thus, the Examiner's reference to the invention being an obvious

ordering of the steps is misplaced. As such, the instant invention is not achieved by the references and withdrawal thereof is respectfully requested.

In addition, as noted by the Examiner, the specification presents comparative data in Table 1, page 30. When comparing the degree of complexation of example 1, which is an example according to the present invention, with the degree of complexation of comparative example 3, which corresponds to the product obtained by the process described in Van Hees (2002), it can be seen that the degree of complexation is higher with the instant invention.

The Examiner considers that such a difference of degree of complexation is predictable because ammonia is extremely corrosive when used at the supercritical state. The Examiner asserts that one skilled in the art would expect supercritical ammonia to be corrosive on the reactor, resulting in a lower yield.

However, in comparative example 3 and in example 1, the reactor was an autoclave made of stainless steel 316L, which is very resistant to ammonia either in the aqueous, gases or liquor form. (See the Corrosive Data table attached hereto was Exhibit A.) In addition, the inventors did not find any evidence of corrosion of the reactors when making comparative example 3. Thus, contrary to the presumption of the Examiner, the lower yield seen with the example of Van Hees (2002) (comparative example 3 of the specification) compared to the instant invention is not the result of the corrosive nature of supercritical ammonia. Therefore, the reactors were not corroded by ammonia and such corrosion has no effect on the degree of complexation. Thus, the differences obtained when comparing example 1 and comparative example 3 are completely unexpected.

The instant invention therefore provides unexpected improved results over the process disclosed in Van Hees (2002). The improved results are in no way suggested by any of the cited references and the instantly claimed invention is therefore not obvious over Van Hees et al (2002) combined with Van Hees (1999) and Junco. Withdrawal of the rejection is, therefore, respectfully requested.

Obviousness-type double patenting

Claims 11-22 have been provisionally rejected under judicially created doctrine of obviousness-type double patenting as being obvious over claims 1-10 and 13 of co-pending application No. 10/554,058 in view of Van Hees (2002).

Claims 11-12 have further been provisionally rejected under judicially created doctrine of obviousness-type double patenting as being obvious over claims 1 and 8-14 of co-pending application No. 10/492,346 in view of Van Hees (2002).

Applicants traverse these rejections and withdrawal thereof is respectfully requested. The '058 and '346 applications, as well as Van Hees (2002), all disclose only a single step. As described above, the process according to the present invention is a two step process in which the addition of the agent of interaction is carried out after the formation of the complex. None of the documents of the prior art suggests using a process having two steps. As such, the instant invention is neither taught nor suggested by the '058 or '346 applications when considered alone or in combination with Van Hees (2002).

As further discussed above, the instant invention possesses unexpected improved properties. As such, withdrawal of the instant invention possesses unexpected improved properties. As such, withdrawal of the obviousness-type double patenting rejection is respectfully requested.

However, in the event that the Examiner chooses not to withdraw the rejections at this time, Applicants respectfully request that these issues be held in abeyance until the claims in one of the two applications are otherwise allowable.

As the above amendments and Remarks address and overcome the rejections, withdrawal thereof and allowance of the claims are respectfully requested.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact MaryAnne Armstrong, Ph.D., Reg. No. 40,069 at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If the Examiner has any questions regarding the instant application, he is requested to please contact MaryAnne Armstrong, PhD (Reg. No. 40,069) at the phone number indicated below.

Dated: October 14, 2008

Respectfully submitted,

By ____________________

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Attachments: Exhibit A

Exhibit A

CORROSION DATA

CHEMICALS	Brass	Carbon Steel	316 Stainless Steel	Teflon Reinforced
Acetaldehyde	C	C	A	A
Acetamine	B	B	B	A
Acetate Solvents	B	A	A	A
Acetic Acid,aerated	D	D	A	A
Acetic Acid,Air Free	B	D	A	A
Acetic Acid,crude	C	C	A	A
Acetic Acid,glacial				A
Acetic Acid,pure	C	D	A	A
Acetic Acid,10%	C	C	A	A
Acetic Acid,80%	C	C	A	A
Acetic Acid Vapors	D		D	A
Acetic Anhydride	D	D	B	A
Acetone	A	A	A	A
Other Ketones	A	A	A	A
Acetyl Chloride	A		C	A
Acetylene	B	A	A	A
Acid Fumes	D	D	B	A
Acrylonite	A	A	A	A
Air	A	A	A	A
Alcohol, Amyl	B	B	A	A
Alcohol, Butyl	B	B	A	A
Alcohol, Diacetone	A	A	A	A
Alcohol, Ethyl	B	B	B	A
Alcohol, Fatty	B	B	A	A
Alcohol, Isopropyl	B	B	B	A
Alcohol, Methyl	B	B	A	A
Alcohol, Propyl	A	B	A	A
Alumina	A			A
Aluminum Acetate	D		A	A
Aluminum Chloride dry	B	C	C	A
Aluminum Chloride solution			D	A
Aluminum Fluoride		D	C	A
Aluminum Hydroxide	A	D	A	A
Aluminum Nitrate	D		C	A
Aluminum Oxalate				A
Alum (Aluminum Potassium Sulfate)	D		B	A
Alum (Aluminum Sulfate)	C	D	B	A
Amines	B	B	A	A
Ammonia, Alum			A	A
Ammonia, Anhydrous Liquid	D	A	A	A
Ammonia, Aqueous	D	A	A	A
Ammonia, Gas, hot	D		A	A
Ammonia Liquor			A	A
Ammonia Solutions	D	B	A	A
Ammonium Acetate	D		B	A
Ammonium Bicarbonate	B	C	B	A
Ammonium Bromide 5%			B	A
Ammonium Carbonate	B	B	B	A
Ammonium Chloride	D	D	C	A
Ammonium Hydroxide 28%	D	C	B	A
Ammonium Hydroxide Concentrated	D	C	B	A
Ammonium Monosulfate			A	A
Ammonium Nitrate	D	D	A	A

Ratings: **A**-Excellent **B**-Good **C**-Poor **D**-Do not use **Blank**-No Information

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Metals and Corrosion Resistance

Common metals and their corrosion resistance to aggressive fluids as acids, bases and more

A major problem in the process industry is the corrosion of metals in pipes, valves and other parts of the constructions. This guide indicates acceptable combinations of more or less aggressive fluids and commonly used materials.

Note! Remember that corrosion is a complicated issue, depending on the combinations of materials and the fluids, the fluid temperatures, the surrounding environment and the galvanic currents in the constructions. The table below must be used with care. Always check with the producer of the material.

Corrosion Resistance 1) Good 2) Be Careful 3) Not Useable

Fluid	Metal											
	Carbon Steel	Cast Iron	302 and 304 Stainless Steel	316 Stainless Steel	Bronze	Durimet	Monel	Hasteloy B	Hasteloy C	Titanium	Cobalt base alloy 6	416 Stainless Steel
Acetaldehyde	1	1	1	1	1	1	1	na	1	na	na	1
Acetic acid, air free	3	3	2	2	2	1	2	1	1	1	1	3
Acetic acid, aerated	3	3	1	1	1	1	1	1	1	1	1	3
Acetic acid, vapors	3	3	1	1	2	2	2	na	1	1	1	3
Acetone	1	1	1	1	1	1	1	1	1	1	1	1
Acetylene	1	1	1	1		1	1	1	1	na	1	1
Alcohols	1	1		1	1	1	1	1	1	1	1	1
Aluminum Sulfate	3	3	1	1	2	1	2	1	1	1	na	3
Ammonia	1	1	1	1	3	1	3	1	1	1	1	1
Ammonium chloride	3	3	2	2	2	1	2	1	1	1	2	3
Ammonium Nitrate	1	3	1	1	3	1	3	1	1	1	1	3
Ammonium Phosphate	4	3	1	1	2	2	2	1	1	1	1	2
Ammonium Sulfate	3	3	2	1	2	1	1	1	1	1	1	3
Ammonium Sulfite	3	3	1	1	3	1	3	na	1	1	1	2
Aniline	3	3	1	1	3	1	2	1	1	1	1	3
Asphalt	1	1	1	1	1	1	1	1	1	na	1	1
Beer	2	2	1	1	2	1	1	1	1	1	1	2
Benzene (benzol)	1	1	1	1	1	1	1	1	1	1	1	1
Benzoic acid	3	3	1	1	1	1	1		1	1		1
Boric acid	3	3	1	1	1	1	1	1	1	1	1	2
Butane	1	1	1	1	1	1	1	1	1		1	1
Calcium Chloride (alkaline)	2	2	3	2	3	1	1	1	1	1	na	3
Calcium hypochlorite	3	3	2	2	2	1	2	3	1	1	na	3
Carbolic acid	2	2	1	1	1	1	1	1	1	1	1	
Carbon dioxide, dry	1	1	1	1	1	1	1	1	1	1	1	1

Carbonic acid	3	3	2	2	2	1	1	1	1			1
Chlorine gas	1	1	2	2	2	1	1	1	1	3	2	3
Chlorine gas, wet	3	3	3	3	3	3	3	3	2	1	2	3
Chlorine, liquid	3	3	3	3	2	2	3	3	1	3	2	3
Chromic acid	3	3	3	2	3	3	1	3	1	1	2	3
Citric acid		3	2	1	1	1	2	1	1	1		2
Coke oven gas	1	1	1	1	2	1	2	1	1	1	1	1
Copper sulfate	3	3	2	2	2	1	3	na	1	1	na	1
Cottonseed oil	1	1	1	1	1	1	1	1	1	1	1	1
Creosote	1	1	1	1	3	1	1	1	1		1	1
Ethane	1	1	1	1	1	1	1	1	1	1	1	1
Ether	2	2	1	1	1	1	1	1	1	1	1	1
Ethyl chloride	3	3	1	1	1	1	1	1	1	1	1	2
Ethylene	1	1	1	1	1	1	1	1	1	1	1	1
Ethylene glycol	1	1	1	1	1	1	1	na	na	na	1	1
Ferric chloride	3	3	3	3	3	3	3	3	2	1	2	3
Formaldehyde	2	2	1	1	1	1	1	1	1	1	1	1
Formic acid		3	2	2	1	1	1	1	1	3	2	3
Freon wet	2	2	2	1	1	1	1	1	1	1	1	na
Freon dry	2	2	1	1	1	1	1	1	1	1	1	na
Furfural	1	1	1	1	1	1	1	1	1	1	1	2
Gasoline	1	1	1	1	1	1	1	1	1	1	1	1
Glucose	1	1	1	1	1	1	1	1	1	1	1	1
Hydrochloric acid, aerated	3	3	3	3	3	3	3	1	2	3	2	3
Hydrochloric acid, air free	3	3	3	3	3	3	3	1	2	3	2	3
Hydrofluoric acid, aerated	2	3	3	2	3	2	3	1	1	3	2	3
Hydrofluoric acid, air free	1	3	3	2	3	2	1	1	1	3	na	3
Hydrogen	1	1	1	1	1	1	1	1	1	1	1	1
Hydrogen peroxide		1	1	1	3	1	3	2	2	1	na	2
Hydrogen sulfide, liquid	3	3	1	1	3	2	3	1	1	1	1	3
Magnesium Hydroxide	1	1	1	1	2	1	1	1	1	1	1	1
Mercury	1	1	1	1	3	1	2	1	1	1	1	1
Methanol	1	1	1	1	1	1	1	1	1	1	1	1
Methyl ethyl ketone	1	1	1	1	1	1	1	1	1		1	1
Milk	3	3	1	1	1	1	1	1	1	1	1	3
Natural gas	1	1	1	1	1	1	1	1	1	1	1	1
Nitric acid	3	3	1	2	3	1	3	3	2	1	3	3
Oleic acid	3	3	1	1	2	1	1	1	1	1	1	1
Oxalic acid	3	3	2	2	2	1	2	1	1	2	2	2
Oxygen	1	1	1	1	1	1	1	1	1	1	1	1
Petroleum oils	1	1	1	1	1	1	1	1	1	1	1	1
Phosphoric acid, aerated	3	3	1	1	3	1	3	1	1	2	1	3
Phosphoric acid, air free	3	3	1	1	3	1	2	1	1	2	1	3
Phosphoric acid vapors	3	3	2	2	3	1	3	1		2	3	3
Picric acid	3	3	1	1	3	1	3	1	1	na	na	2

Rosin	2	2	1	1	1	1	1	1	1		1	1
Silver Nitrate	3	3	1	1	3	1	3	1	1	1	2	2
Sodium acetate	1	1	2	1	1	1	1	1	1	1	1	1
Sodium carbonate	1	1	1	1	1	1	1	1	1	1	1	2
Sodium chloride	3	3	2	2	1	1	1	1	1	1	1	2
Sodium chromate	1	1	1	1	1	1	1	1	1	1	1	1
Sodium hydroxide	1	1	1	1	3	1	1	1	1	1	1	2
Sodium hypochloride	3	3	3	3	3	2	3	3	1	1	na	3
Sodium thiosulfate	3	3	1	1	3	1	3	1	1	1	na	2
Stannous chloride	2	2	3	1	3	1	2	1	1	1	na	3
Stearic acid	1	3	1	1	2	1	2	1	1	1	2	2
Sulfate liquor	1	1	1	1	3	1	1	1	1	1	1	
Sulfur	1	1	1	1	3	1	1	1	1	1	1	1
Sulfur dioxide, dry	1	1	1	1	1	1	1	2	1	1	1	2
Sulfur trioxide, dry	1	1	1	1	1	1	1	2	1	1	1	2
Sulfuric acid, aerated	3	3	3	3	3	1	3	1	1	2	2	3
Sulfuric acid, air free	3	3	3	3	2	1	2	1	1	2	2	3
Sulfurous acid	3	3	2	2	2	1	3	1	1	1	2	3
Tar	1	1	1	1	1	1	1	1	1	1	1	1
Trichloroethylene	2	2	2	1	1	1	1	1	1	1	1	2
Turpentine	2	2	1	1	1	1	2	1	1	1	1	1
Vinegar	3	3	1	1	2	1	1	1	1	na	1	3
Water, steam boiler feeding system	2	3	1	1	3	1	1	1	1	1	1	2
Water, distilled	1	1	1	1	1	1	1	1	1	1	1	2
Water, sea	2	2	2	2	1	1	1	1	1	1	1	3
Whiskey	3	3	1	1	1	1	2	1	1	1	1	3
Wine	3	3	1	1	1	1	2	1	1	1	1	3
Zinc chloride	3	3	3	3	3	1	3	1	1	1	2	3
Zinc sulfate	3	3	1	1	2	1	1	1	1	1	1	2

- na - data not available

Related Topics

- Material Properties Material properties - density, heat capacity, viscosity and more - for gases, fluids and solids
- Design Strategy of Piping Systems Piping systems and engineering related topics - documentation, P&ID, flow diagrams - capacities and limits
- Control Valves Control Valve terminology, bodies, trim, flow characteristics, Cv and Kv sizing, noise, actuators and positioners